

# CLAIMS

What is claimed is:

5

1. A compound of Formula I



I

or a pharmaceutically acceptable salt thereof,

wherein:

10

Z is selected from:

HO<sub>2</sub>C;

HO(H)N(O)C;

H(O)C-N(OH);

CH<sub>3</sub>(O)C-N(OH);

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CH<sub>3</sub>(H)N(O)C-N(OH);

HS;

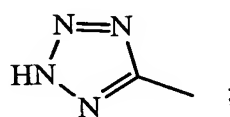
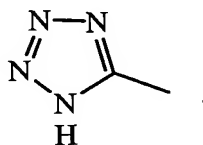
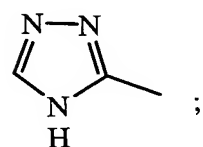
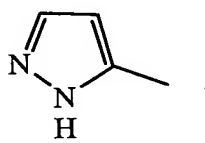
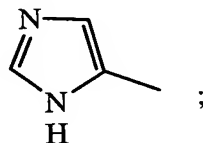
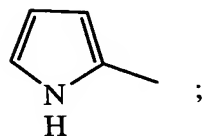
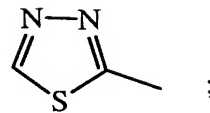
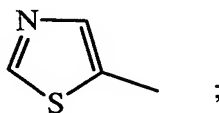
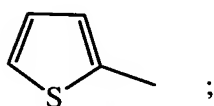
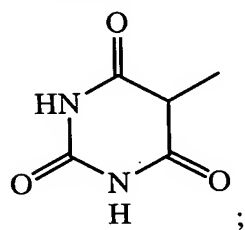
H<sub>2</sub>N(O)<sub>2</sub>S;

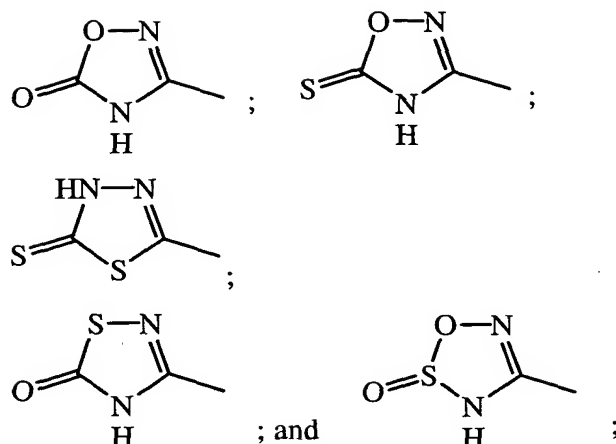
CH<sub>3</sub>(H)N(O)<sub>2</sub>S;

HO(O)P;

20

(HO)<sub>2</sub>(O)P;





L is selected from:

- 5             $C_3$ - $C_5$  alkylenyl;
- Substituted  $C_3$ - $C_5$  alkylenyl;
- 3- to 5-membered heteroalkylenyl; and
- Substituted 3- to 5-membered heteroalkylenyl;

10           Substituted L groups contain 1 or 2 substituents on a carbon atom or nitrogen atom independently selected from:

- HO;
- CN; and
- $CF_3$ ;

15           wherein each substituent on a carbon atom may further be independently F, and wherein 2 substituents may be taken together with a carbon atom to which they are both bonded to form the group  $C=O$ ;

$R^1$  is independently selected from:

- $C_5$  or  $C_6$  cycloalkylenyl- $(C_1-C_8$  alkylenyl);
- Substituted  $C_5$  or  $C_6$  cycloalkylenyl- $(C_1-C_8$  alkylenyl);
- 20           5- or 6-membered heterocycloalkylenyl- $(C_1-C_8$  alkylenyl);
- Substituted 5- or 6-membered heterocycloalkylenyl- $(C_1-C_8$  alkylenyl);
- Phenylenyl- $(C_1-C_8$  alkylenyl);
- Substituted phenylenyl- $(C_1-C_8$  alkylenyl);
- 5- or 6-membered heteroarylenyl- $(C_1-C_8$  alkylenyl);
- 25           Substituted 5- or 6-membered heteroarylenyl- $(C_1-C_8$  alkylenyl);
- Phenyl;

Substituted phenyl;  
Naphthyl;  
Substituted naphthyl;  
5- or 6-membered heteroaryl;  
5 Substituted 5- or 6-membered heteroaryl;  
8- to 10-membered heterobiaryl; and  
Substituted 8- to 10-membered heterobiaryl;

$R^2$  is independently selected from:

H;  
10  $C_1$ - $C_6$  alkyl;  
Phenyl-( $C_1$ - $C_8$  alkylene);  
Substituted phenyl-( $C_1$ - $C_8$  alkylene);  
Naphthyl-( $C_1$ - $C_8$  alkylene);  
Substituted naphthyl-( $C_1$ - $C_8$  alkylene);  
15 5- or 6-membered heteroaryl-( $C_1$ - $C_8$  alkylene);  
Substituted 5- or 6-membered heteroaryl-( $C_1$ - $C_8$  alkylene);  
8- to 10-membered heterobiaryl-( $C_1$ - $C_8$  alkylene);  
Substituted 8- to 10-membered heterobiaryl-( $C_1$ - $C_8$  alkylene);  
Phenyl-O-( $C_1$ - $C_8$  alkylene);  
20 Substituted phenyl-O-( $C_1$ - $C_8$  alkylene);  
Phenyl-S-( $C_1$ - $C_8$  alkylene);  
Substituted phenyl-S-( $C_1$ - $C_8$  alkylene);  
Phenyl-S(O)-( $C_1$ - $C_8$  alkylene);  
Substituted phenyl-S(O)-( $C_1$ - $C_8$  alkylene);  
25 Phenyl-S(O)<sub>2</sub>-( $C_1$ - $C_8$  alkylene); and  
Substituted phenyl-S(O)<sub>2</sub>-( $C_1$ - $C_8$  alkylene);

Each substituted  $R^1$  group contains from 1 to 3 substituents, and each substituted  $R^2$  group contains from 1 to 4 substituents, wherein each substituent is independently on a carbon or nitrogen atom, independently selected from:

30  $C_1$ - $C_6$  alkyl;  
CN;  
CF<sub>3</sub>;  
HO;

(C<sub>1</sub>-C<sub>6</sub> alkyl)-O;

(C<sub>1</sub>-C<sub>6</sub> alkyl)-S(O)<sub>2</sub>;

H<sub>2</sub>N;

(C<sub>1</sub>-C<sub>6</sub> alkyl)-N(H);

5

(C<sub>1</sub>-C<sub>6</sub> alkyl)<sub>2</sub>-N;

(C<sub>1</sub>-C<sub>6</sub> alkyl)-C(O)O-(C<sub>1</sub>-C<sub>8</sub> alkylenyl)<sub>m</sub>;

(C<sub>1</sub>-C<sub>6</sub> alkyl)-C(O)O-(1- to 8-membered heteroalkylenyl)<sub>m</sub>;

(C<sub>1</sub>-C<sub>6</sub> alkyl)-C(O)N(H)-(C<sub>1</sub>-C<sub>8</sub> alkylenyl)<sub>m</sub>;

(C<sub>1</sub>-C<sub>6</sub> alkyl)-C(O)N(H)-(1- to 8-membered heteroalkylenyl)<sub>m</sub>;

10

H<sub>2</sub>NS(O)<sub>2</sub>-(C<sub>1</sub>-C<sub>8</sub> alkylenyl);

(C<sub>1</sub>-C<sub>6</sub> alkyl)-N(H)S(O)<sub>2</sub>-(C<sub>1</sub>-C<sub>8</sub> alkylenyl)<sub>m</sub>;

(C<sub>1</sub>-C<sub>6</sub> alkyl)<sub>2</sub>-NS(O)<sub>2</sub>-(C<sub>1</sub>-C<sub>8</sub> alkylenyl)<sub>m</sub>;

3- to 6-membered heterocycloalkyl-(G)<sub>m</sub>;

Substituted 3- to 6-membered heterocycloalkyl-(G)<sub>m</sub>;

15

5- or 6-membered heteroaryl-(G)<sub>m</sub>;

Substituted 5- or 6-membered heteroaryl-(G)<sub>m</sub>;

(C<sub>1</sub>-C<sub>6</sub> alkyl)-S(O)<sub>2</sub>-N(H)-C(O)-(C<sub>1</sub>-C<sub>8</sub> alkylenyl)<sub>m</sub>; and

(C<sub>1</sub>-C<sub>6</sub> alkyl)-C(O)-N(H)-S(O)<sub>2</sub>-(C<sub>1</sub>-C<sub>8</sub> alkylenyl)<sub>m</sub>;

wherein each substituent on a carbon atom may further be independently selected from:

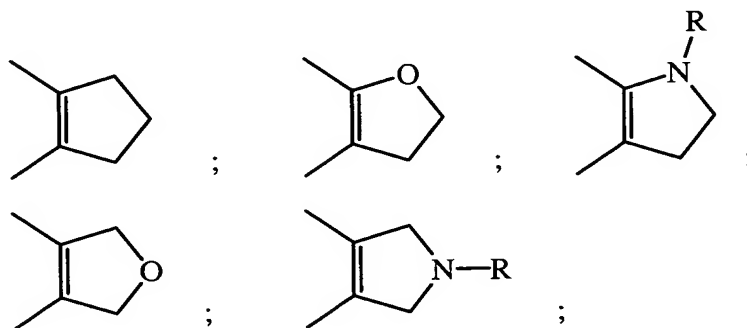
Halo; and

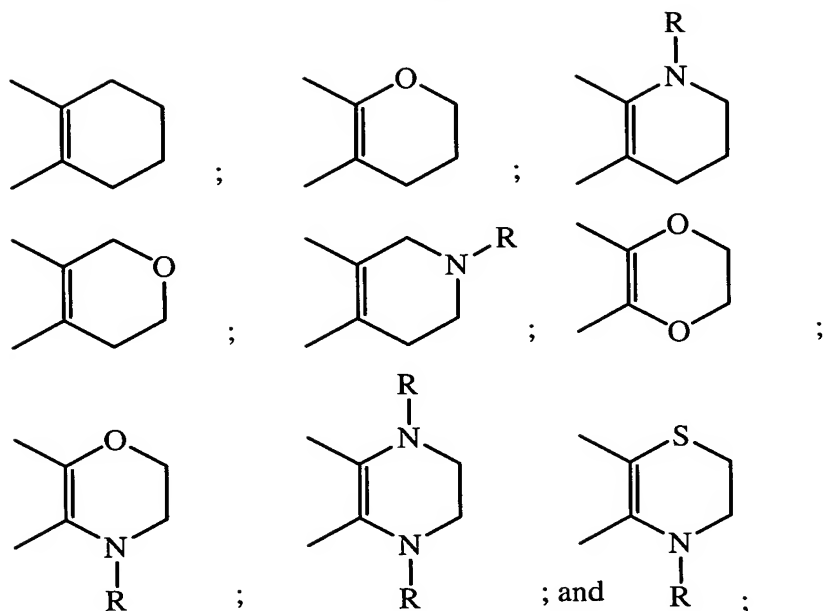
HO<sub>2</sub>C;

wherein 2 substituents may be taken together with a carbon atom to which they are both bonded to form the group C=O;

25

wherein two adjacent, substantially sp<sup>2</sup> carbon atoms may be taken together with a diradical substituent to form a cyclic diradical selected from:





R is H or C<sub>1</sub>-C<sub>6</sub> alkyl;

5 G is CH<sub>2</sub>; O, S, S(O); or S(O)<sub>2</sub>;

Each m is an integer of 0 or 1;

Q, when bonded to a nitrogen atom in group D, is selected from:

OC(O);

CH(R<sup>6</sup>)C(O);

10 OC(NR<sup>6</sup>);

CH(R<sup>6</sup>)C(NR<sup>6</sup>);

N(R<sup>6</sup>)C(O);

N(R<sup>6</sup>)C(S);

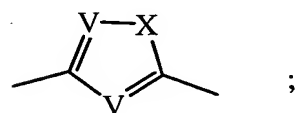
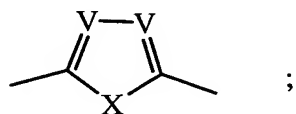
N(R<sup>6</sup>)C(NR<sup>6</sup>);

15 SC(O);

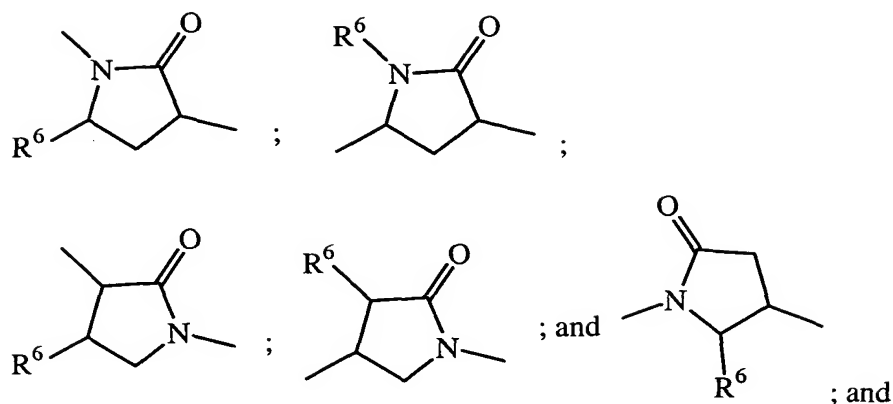
CH(R<sup>6</sup>)C(S);

SC(NR<sup>6</sup>);

C≡CCH<sub>2</sub>;



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Q, when bonded to a carbon atom in group D, is as defined above and may further be selected from:

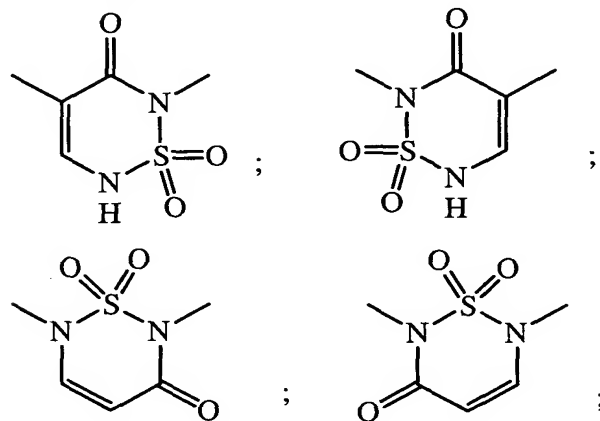
- 5  $\text{OCH}_2$ ;
- $\text{N(R}^6\text{)CH}_2$ ;
- $\text{trans-(H)C=C(H)}$ ;
- $\text{cis-(H)C=C(H)}$ ;
- $\text{C}\equiv\text{C}$ ;
- $\text{CH}_2\text{C}\equiv\text{C}$ ;
- 10  $\text{CF}_2\text{C}\equiv\text{C}$ ;
- $\text{C}\equiv\text{CCF}_2$ ;

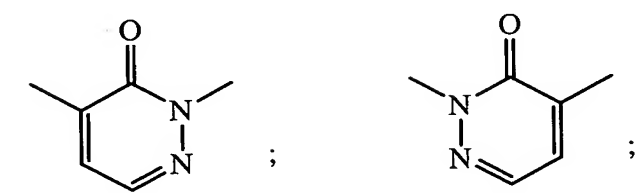
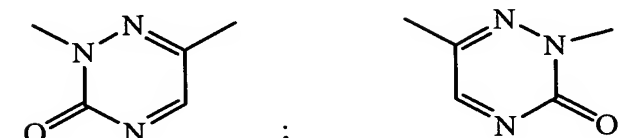
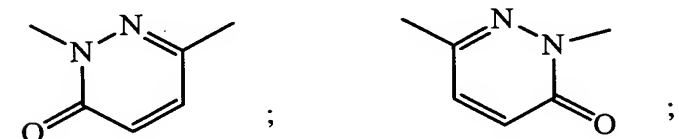
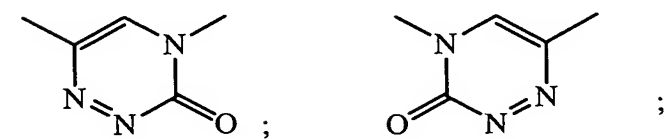
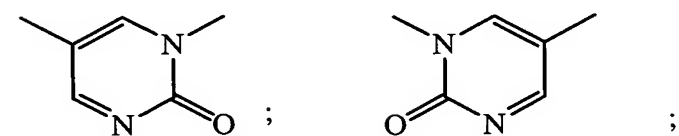
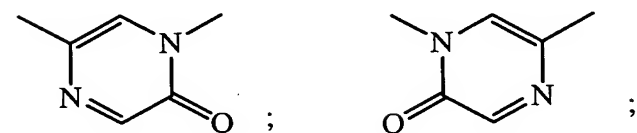
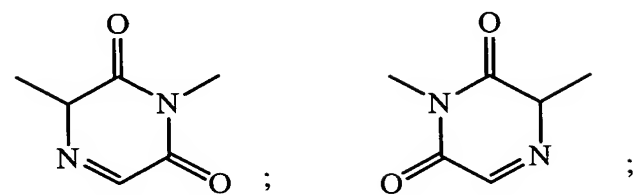
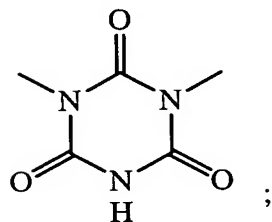
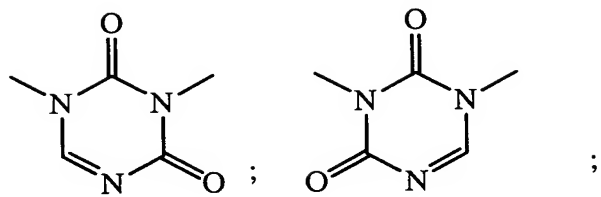
Each  $\text{R}^6$  independently is H,  $\text{C}_1\text{-C}_6$  alkyl,  $\text{C}_3\text{-C}_6$  cycloalkyl; 3- to 6-membered heterocycloalkyl; phenyl; benzyl; or 5- or 6-membered heteroaryl;

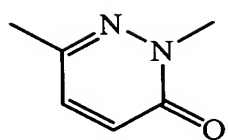
X is O, S, N(H), or N( $\text{C}_1\text{-C}_6$  alkyl);

- 15 Each V is independently C(H) or N;

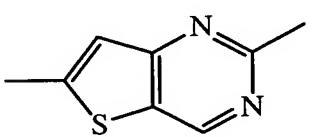
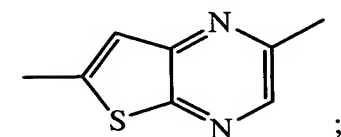
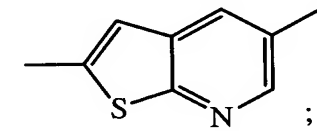
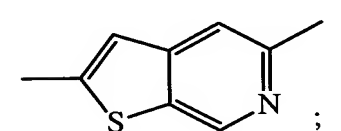
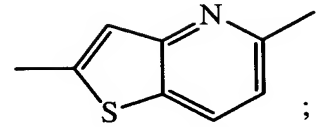
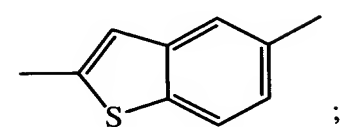
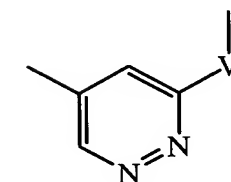
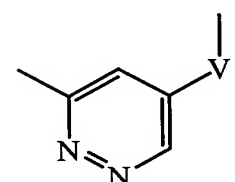
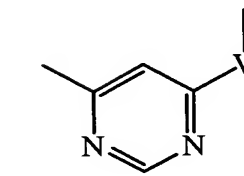
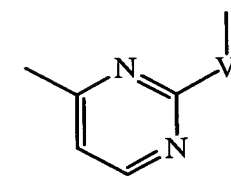
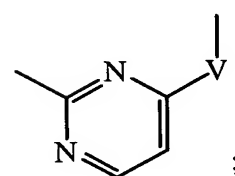
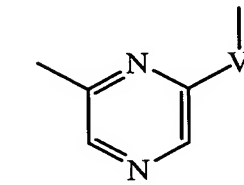
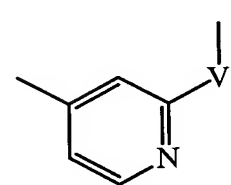
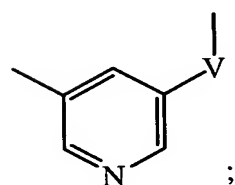
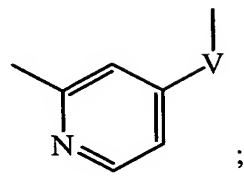
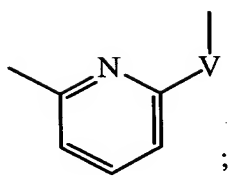
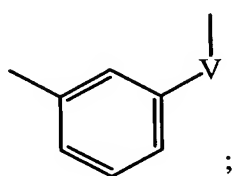
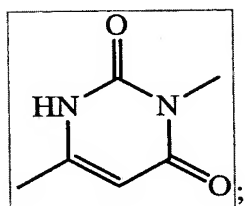
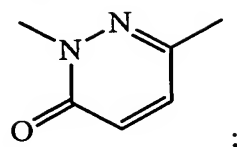
D is a cyclic diradical group selected from:



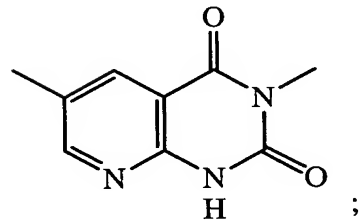
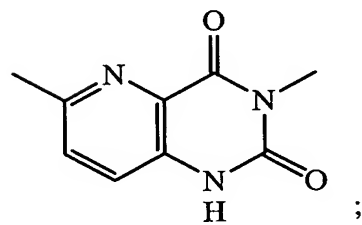
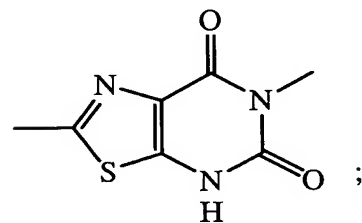
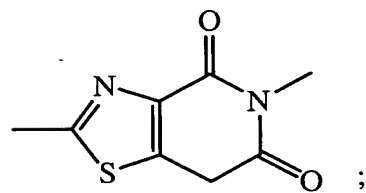
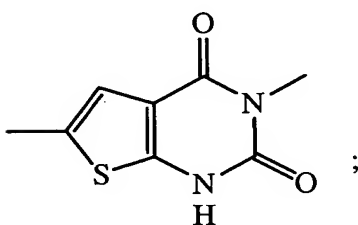
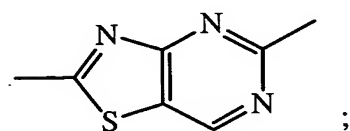
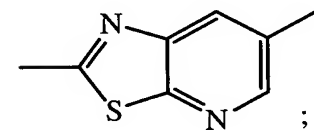
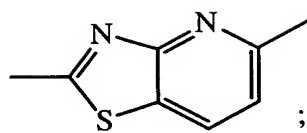
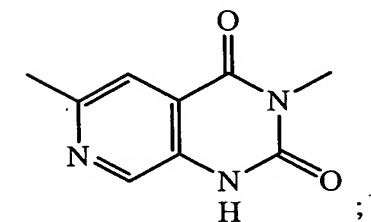
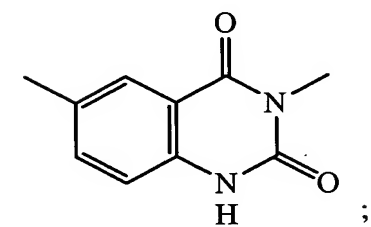
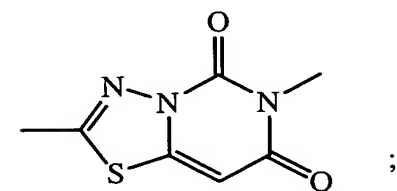
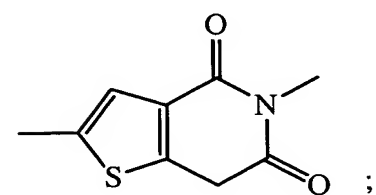
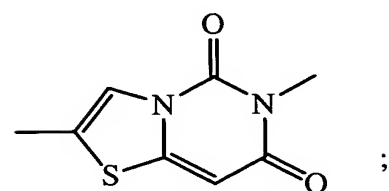
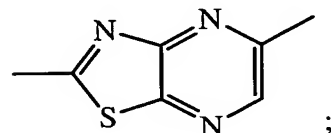
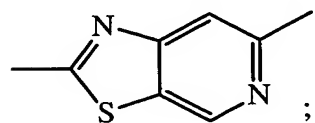
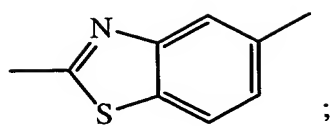


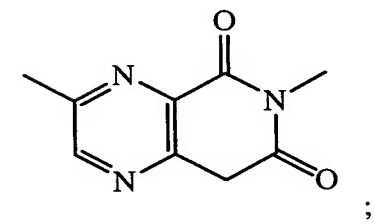
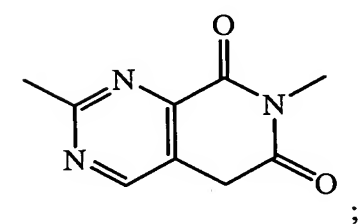
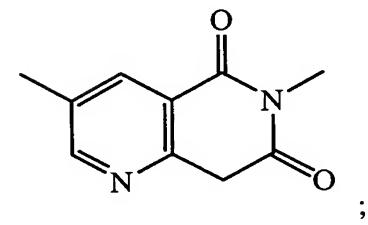
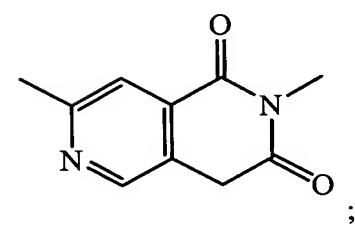
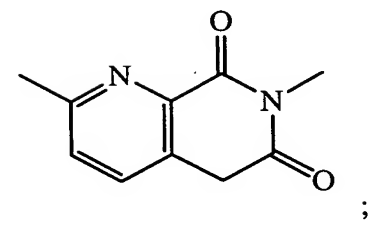
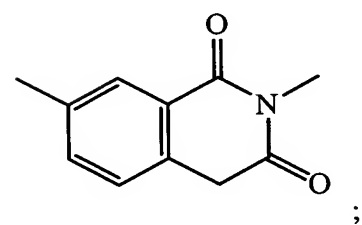
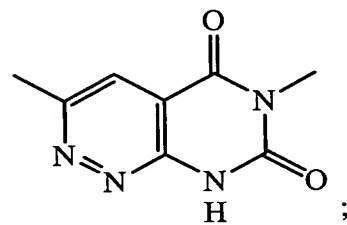
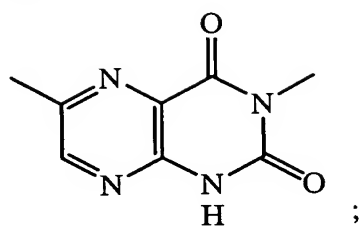
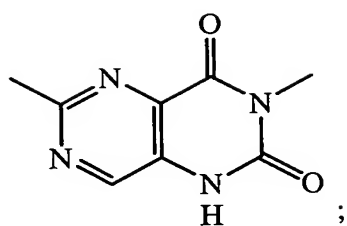


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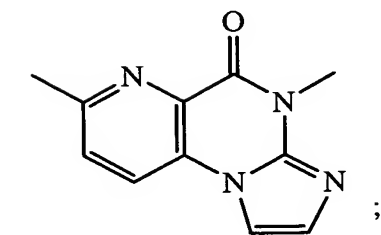
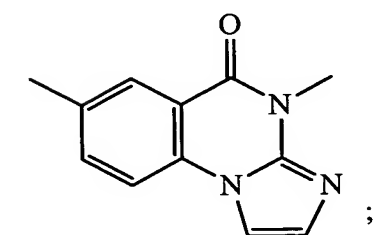
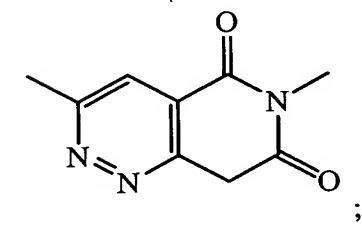


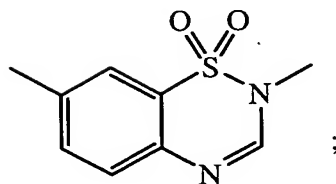
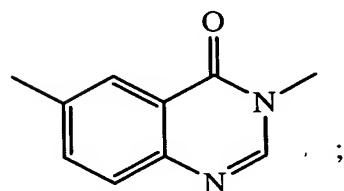
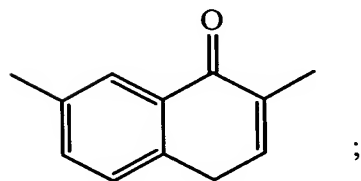
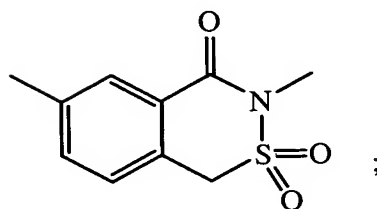
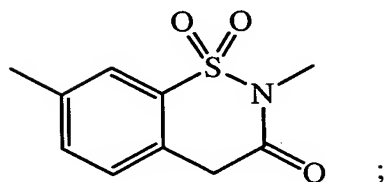
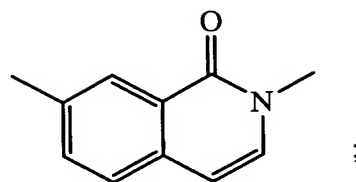
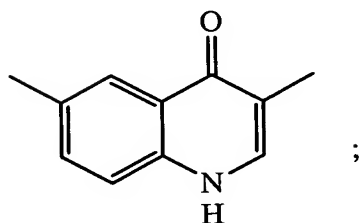
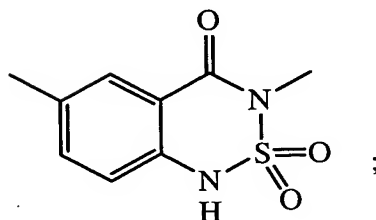
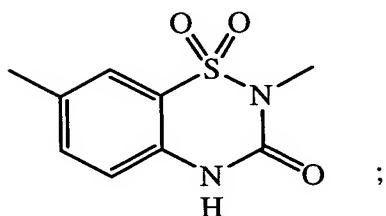
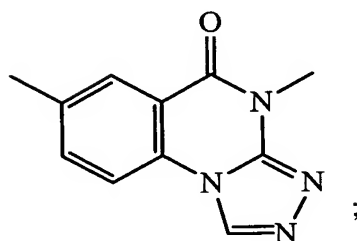
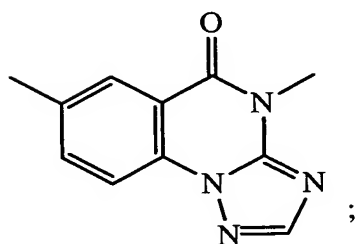
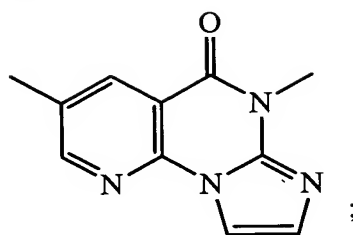
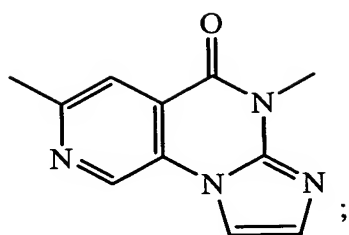


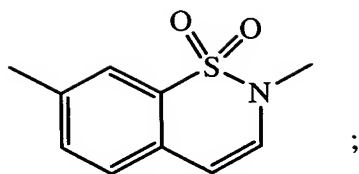




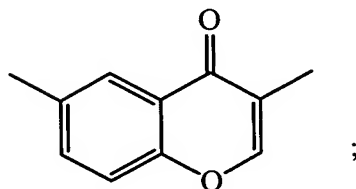
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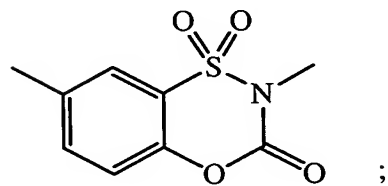




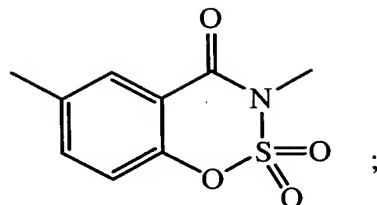
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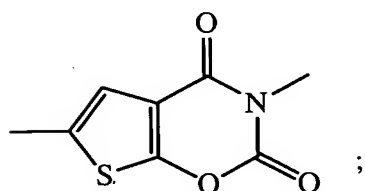
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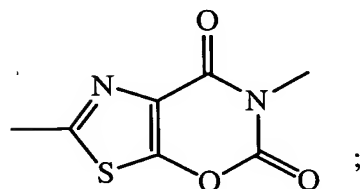
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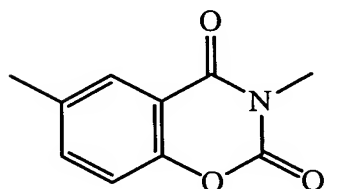
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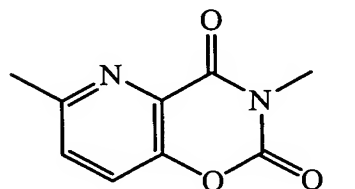
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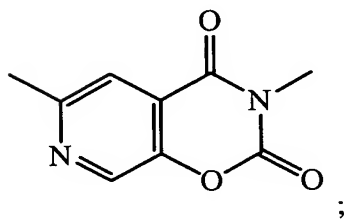
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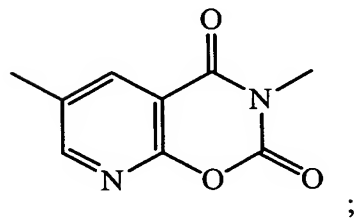
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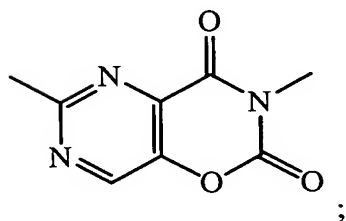
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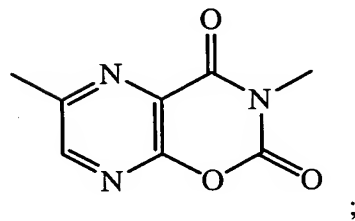
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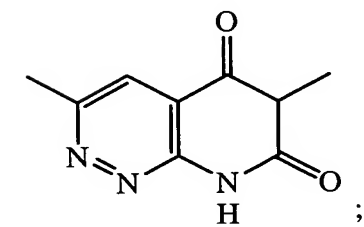
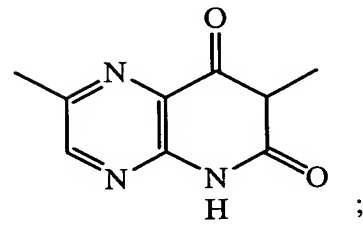
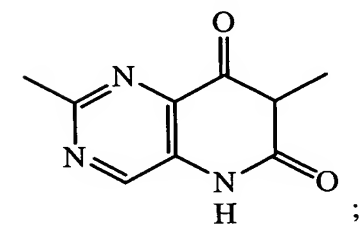
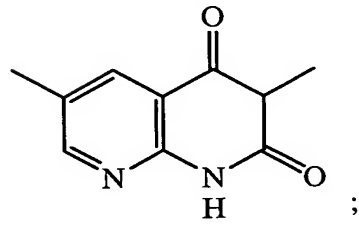
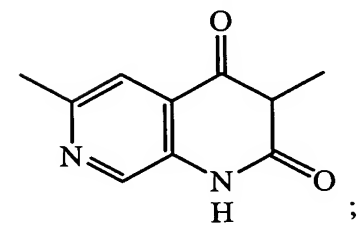
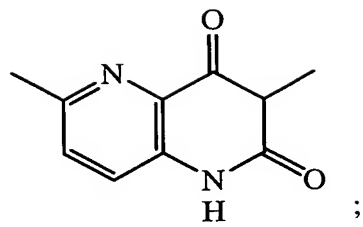
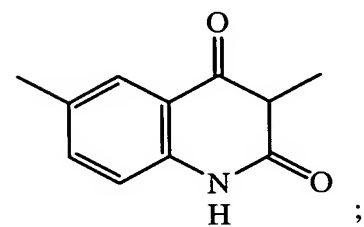
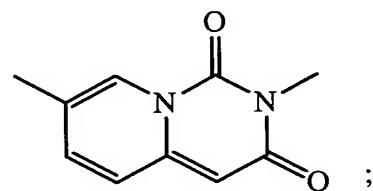
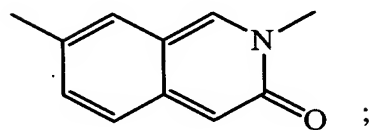
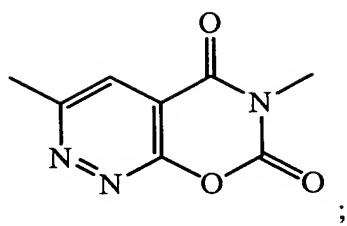
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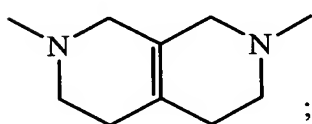
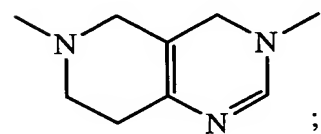
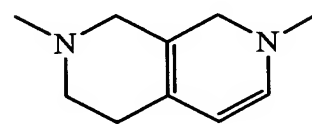
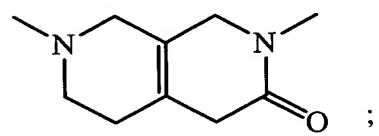
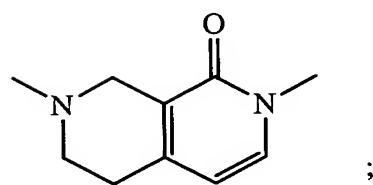
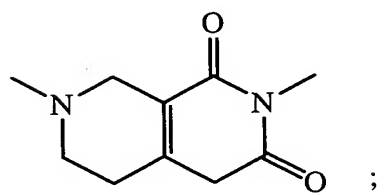
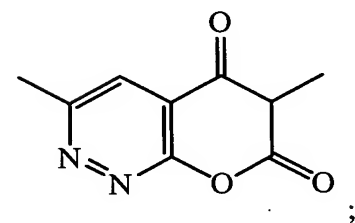
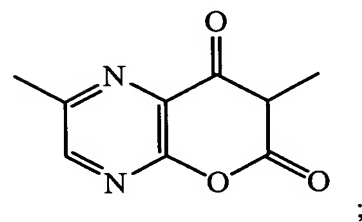
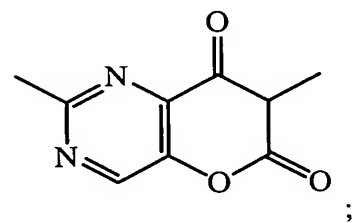
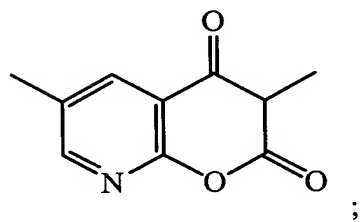
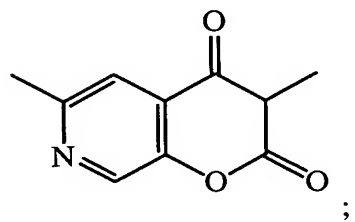
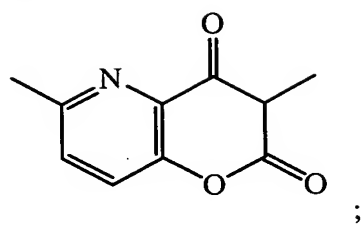
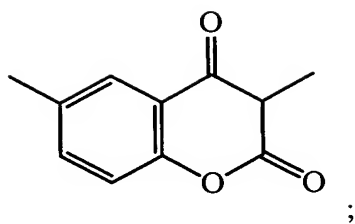


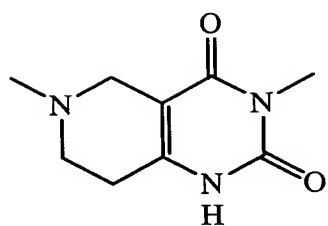
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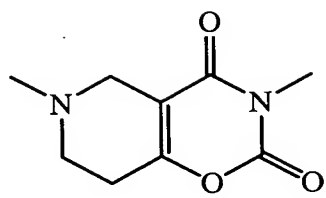
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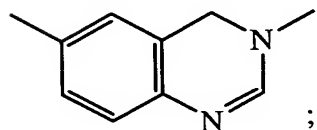




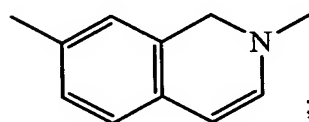
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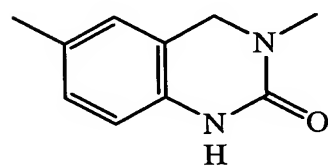
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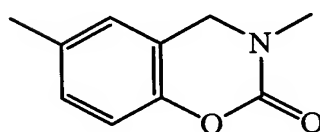
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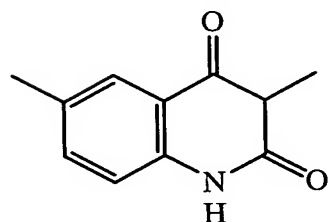
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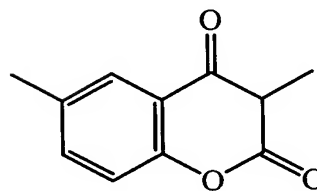
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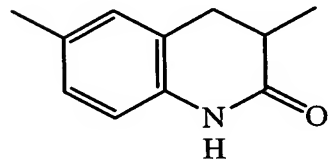
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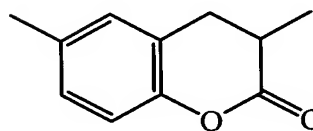
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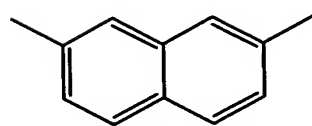


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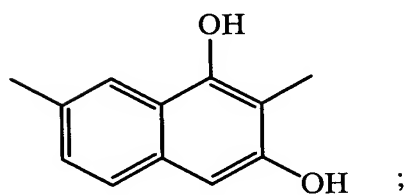


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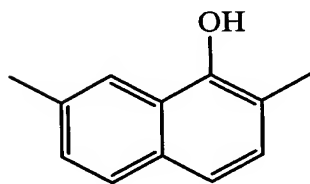
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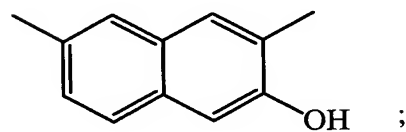
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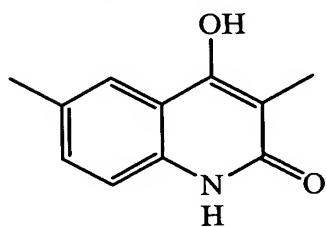
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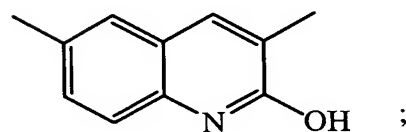
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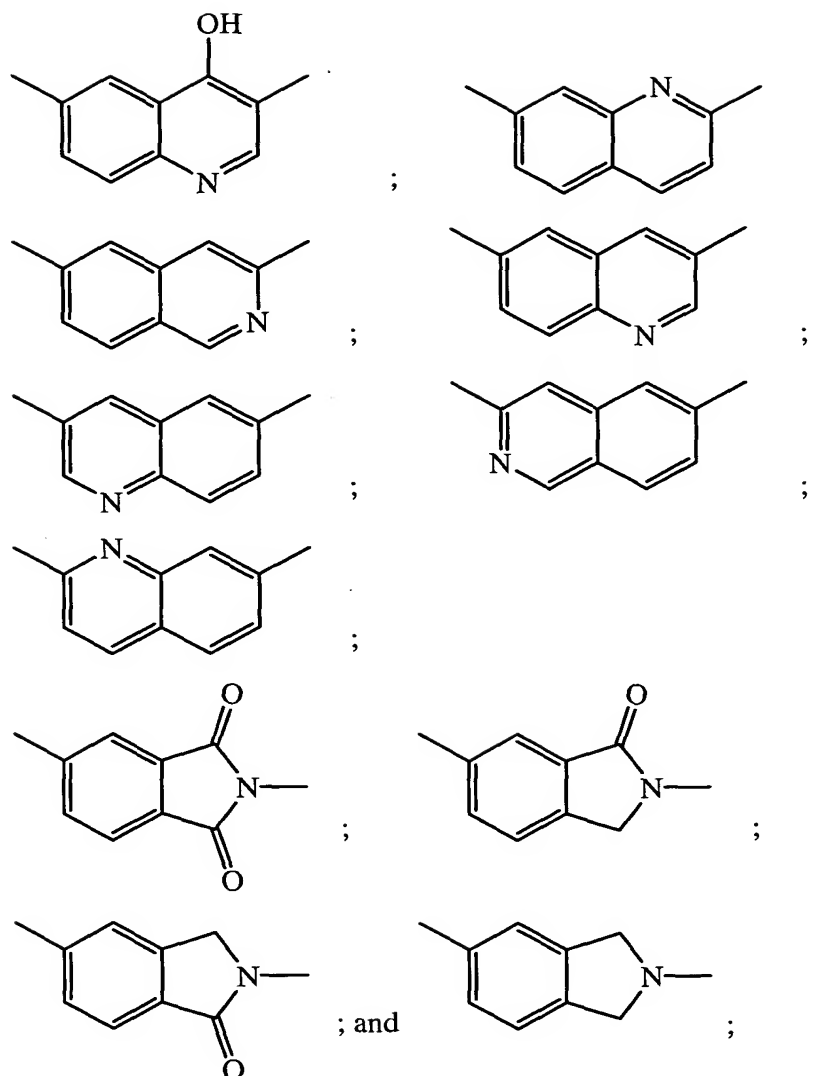
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wherein the group D may be unsubstituted or substituted on a carbon atom or a nitrogen atom by replacement of a hydrogen atom with a group selected from:

CH<sub>3</sub>;

CF<sub>3</sub>;

C(O)H;

CN;

HO;

CH<sub>3</sub>O;

C(F)H<sub>2</sub>O;

C(H)F<sub>2</sub>O; and

CF<sub>3</sub>O;



wherein a carbon atom in the group D may further be substituted with F;

V<sup>1</sup> is a 5-membered heteroarylenyl containing carbon atoms and from 1 to 4

heteroatoms selected from 1 O, 1 S, 1 NH, 1 N(C<sub>1</sub>-C<sub>6</sub> alkyl), and 4 N,

wherein the O and S atoms are not both present, and wherein the

5 heteroarylenyl may optionally be unsubstituted or substituted with 1  
substituent selected from fluoro, methyl, hydroxy, trifluoromethyl, cyano,  
and acetyl;

wherein each C<sub>8</sub>-C<sub>10</sub> bicycloalkyl is a bicyclic carbocyclic ring that contains 8-, 9-

, or 10-member carbon atoms which are 5,5-fused, 6,5-fused, or 6,6-fused bicyclic

10 rings, respectively, and wherein the ring is saturated or optionally contains one  
carbon-carbon double bond;

wherein each 8- to 10-membered heterobicycloalkyl is a bicyclic ring that

contains carbon atoms and from 1 to 4 heteroatoms independently selected from 2

O, 1 S, 1 S(O), 1 S(O)<sub>2</sub>, 1 N, 4 N(H), and 4 N(C<sub>1</sub>-C<sub>6</sub> alkyl), and wherein when two

15 O atoms or one O atom and one S atom are present, the two O atoms or one O  
atom and one S atom are not bonded to each other, and wherein the ring is  
saturated or optionally contains one carbon-carbon or carbon-nitrogen double  
bond, and wherein the heterobicycloalkyl is a 5,5-fused, 6,5-fused, or 6,6-fused  
bicyclic ring, respectively,

20 wherein each heterocycloalkyl is a ring that contains carbon atoms and from 1 to 4  
heteroatoms independently selected from 2 O, 1 S, 1 S(O), 1 S(O)<sub>2</sub>, 1 N, 4

N(H), and 4 N(C<sub>1</sub>-C<sub>6</sub> alkyl), and wherein when two O atoms or one O

atom and one S atom are present, the two O atoms or one O atom and one

S atom are not bonded to each other, and wherein the ring is saturated or

25 optionally contains one carbon-carbon or carbon-nitrogen double bond;

wherein each heterocycloalkylenyl is a ring diradical that contains carbon atoms

and from 1 to 3 heteroatoms independently selected from 1 O, 1 S, 1 S(O),

1 S(O)<sub>2</sub>, 1 N, 2 N(H), and 2 N(C<sub>1</sub>-C<sub>6</sub> alkyl), and wherein when one O atom

and one S atom are present, the one O atom and one S atom are not bonded

30 to each other, and wherein the ring is saturated or optionally contains one  
carbon-carbon or carbon-nitrogen double bond;

wherein each 5-membered heteroaryl contains carbon atoms and from 1 to 4 heteroatoms independently selected from 1 O, 1 S, 1 N(H), 1 N(C<sub>1</sub>-C<sub>6</sub> alkyl), and 4 N, and each 6-membered heteroaryl contains carbon atoms and 1 or 2 heteroatoms independently selected from N, N(H), and N(C<sub>1</sub>-C<sub>6</sub> alkyl), and 5- and 6-membered heteroaryl are monocyclic rings;

wherein a 5-membered heteroarylenyl is a 5-membered monocyclic diradical ring that contains carbon atoms and from 1 to 4 heteroatoms independently selected from 1 O, 1 S, 1 N(H), 1 N(C<sub>1</sub>-C<sub>6</sub> alkyl), and 4 N, wherein the 1 O atom and 1 S atom are not both present, and 6-membered heteroarylenyl is a 6-membered monocyclic diradical ring that contains carbon atoms and 1 or 2 heteroatoms independently selected from 2 N;

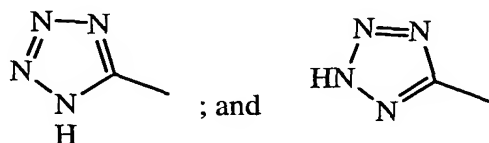
wherein each heterobiaryl contains carbon atoms and from 1 to 4 heteroatoms independently selected from 1 O, 1 S, 1 N(H), 1 N(C<sub>1</sub>-C<sub>6</sub> alkyl), and 4 N, and where the 8-, 9-, and 10-membered heterobiaryl are 5,5-fused, 6,5-fused, and 6,6-fused bicyclic rings, respectively, and wherein at least 1 of the 2 fused rings of a bicyclic ring is aromatic, and wherein when the O and S atoms both are present, the O and S atoms are not bonded to each other;

wherein with any (C<sub>1</sub>-C<sub>6</sub> alkyl)<sub>2</sub>-N group, the C<sub>1</sub>-C<sub>6</sub> alkyl groups may be optionally taken together with the nitrogen atom to which they are attached to form a 5- or 6-membered heterocycloalkyl; and

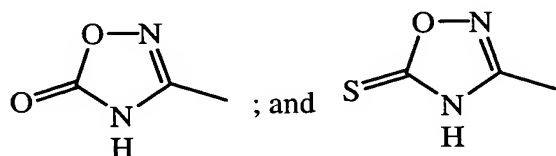
wherein each group and each substituent recited above is independently selected.

2. The compound according to Claim 1, or a pharmaceutically acceptable salt thereof, wherein Z is HO<sub>2</sub>C.

3. The compound according to Claim 1, or a pharmaceutically acceptable salt thereof, wherein Z is selected from:



4. The compound according to Claim 1, or a pharmaceutically acceptable salt thereof, wherein Z is selected from:



5. The compound according to any one of Claims 1 to 4, or a pharmaceutically acceptable salt thereof, wherein Q is  $N(R^6)C(O)$ .
6. The compound according to any one of Claims 1 to 4, or a pharmaceutically acceptable salt thereof, wherein Q is selected from:
- 10  $C\equiv C$ ;  
 $CH_2C\equiv C$ ;  
 $C\equiv CCH_2$ ;  
 $CF_2C\equiv C$ ; and  
 $C\equiv CCF_2$ .
- 15 7. The compound according to Claim 1, selected from:
- 4-(3-{3-[3-(3,4-Difluoro-benzyl)-4-oxo-3,4-dihydro-quinazolin-6-yl]-prop-2-ynyl}-phenyl)-butyric acid; and
- 5-(3,4-Difluoro-benzyl)-7-methyl-4,6-dioxo-3a,4,5,6-tetrahydro-
- 20 thieno[3,2-c]pyridine-2-carboxylic acid [2-(3-mercapto-propoxy)-pyridin-4-ylmethyl]-amide;
- or a pharmaceutically acceptable salt thereof.
8. A pharmaceutical composition, comprising a compound according to
- 25 Claim 1, or a pharmaceutically acceptable salt thereof, admixed with a pharmaceutically acceptable carrier, excipient, or diluent.
9. The pharmaceutical composition according to Claim 8, comprising a compound according to Claim 7, or a pharmaceutically acceptable salt thereof,
- 30 admixed with a pharmaceutically acceptable carrier, excipient, or diluent.

10. A method for treating osteoarthritis, comprising administering to a patient suffering from osteoarthritis or rheumatoid arthritis a nontoxic effective amount of a compound according to Claim 1, or a pharmaceutically acceptable salt thereof.

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11. The method according to Claim 10, wherein the compound administered is a compound according to Claim 7, or a pharmaceutically acceptable salt thereof.

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